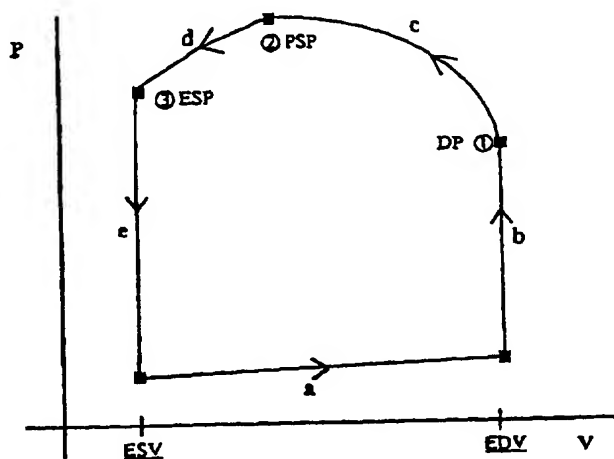




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(54) Title: METHOD AND SYSTEM FOR DETERMINATION OF THE PRESSURE-VOLUME RELATIONSHIP OF THE HEART

**(57) Abstract**

The present invention measures cardiac power and power increase under stress, thus calculating contractile reserve (CR), the difference between cardiac peak power and cardiac power at rest by connecting a person to an electrocardiograph and determining the pressure-volume loop (PVL) of a patient's heart. While deflating an inflated cuff on the person's arm at a controlled rate, a series of data points from peak systolic to diastolic pressure is obtained, each point consisting of cuff pressure at penetration coupled with the time of its occurrence after the corresponding ORS complex; a curve-fitting procedure is applied to turn said data points into a pressure curve resembling the ascending limb of the aortic pressure wave. The end systolic pressure (ESP) is calculated using the expression $ESP = DP + 2/3 (PSP - DP)$, where DP = diastolic pressure and PSP = peak systolic pressure. The volume at point ESP is calculated by integrating said flow curve throughout the ejection phase of the patient's heart.

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METHOD AND SYSTEM FOR DETERMINATION OF THE PRESSURE-VOLUME RELATIONSHIP OF THE HEART

The present invention relates to a method and system for the non-invasive determination of the pressure-volume loop (PVL) of the heart.

The heart, as is known, is a pump and, as such, produces pressure that causes the blood to circulate through the system. A widely used graphic representation of the cardiac function is known as the pressure-volume loop (PVL), referring to the relationship, in the left ventricle, between pressure and volume during a single cardiac cycle which consists of four main phases: (1) the heart being filled with blood; (2) the heart generating enough pressure to overcome arterial resistance; (3) the heart ejecting blood into the arteries, and (4) pressure in the heart dropping so that it is ready to receive blood again.

PVLs have a variety of uses. They have been found to reliably depict various external influences on the heart, such as exercise, drug therapy, cardiac disease, etc. PVLs are an irreplaceable research tool in the field of cardiac mechanics, and are extensively used in the teaching of medical students. Other parameters which can be determined with the aid of the method and system according to the present invention include cardiac power, cardiac peak power and contractile reserve.

Cardiac power, the power of the heart muscle, representing the pumping capability of the heart (in units of work/time), is a known index of the heart's pumping ability [Stein and Sabbah, 1976]. The capability of the heart to increase power has been shown to be directly related to the survival of patients with severe heart failure [Tan, 1987]. Recent studies have shown the cardiac peak power, i.e., the maximum instantaneous cardiac power during blood ejection, to be an accurate descriptor of the

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heart's contractility, the quality of the heart muscle, representing its ability to contract [Kass and Beyar, 1991].

The present invention measures cardiac power as well as power increase under stress, thus calculating contractile reserve (CR), the difference between cardiac peak power and cardiac power at rest. CR can be used to arrive at a prognosis for heart failure patients, and thus to decide the timing of heart transplantation or other therapy. CR is an excellent tool for following the treatment of heart patients and for diagnosing heart disease.

Despite its many uses, no easy way has so far been found to produce PVLs. The only method of doing so until now has been by means of cardiac catheterization, which is an invasive procedure that, as all invasive procedures, puts the patient at a non-negligible risk, is very costly in that it requires a large, highly trained staff, and consequently is not performed in every hospital.

It is thus one of the objects of the present invention to provide a method for determining a patient's PVL by exclusively non-invasive and therefore non-hazardous means, a method that can be applied by a relatively small team of medical personnel mostly on the technician level, and that is therefore within the means of even small medical facilities.

According to the present invention, the above object is achieved by providing a method for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, comprising the steps of connecting said patient to an electrocardiograph; mounting the probe of an echo-Doppler device on the patient in a position enabling it to sense the aortic root and to produce signals

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representative of the flow waves issuing from said aortic root; analyzing said signals and obtaining a series of data points as pairs of flow and time, using the QRS complex of the electrocardiogram pattern as a time reference point; applying a curve-fitting procedure to turn said data points into a flow curve resembling the flow wave issuing from said aortic root; placing a pressure cuff on the patient's arm and inflating it to a point where all flow in the patient's brachial artery stops; deflating said cuff at a controlled rate while measuring pressure inside said cuff throughout deflation; during deflation, sensing blood flow penetrating the barrier constituted by said pressurized cuff, with instantaneous pressure at the aortic root being equal to instantaneous pressure inside said cuff; obtaining a series of data points from peak systolic to diastolic pressure, each point consisting of cuff pressure at penetration coupled with the time of its occurrence after the corresponding QRS complex; applying a curve-fitting procedure to turn said data points into a pressure curve resembling the ascending limb of the aortic pressure wave; calculating the end systolic pressure (ESP) using the expression $ESP = DP + 2/3 (PSP - DP)$, where DP = diastolic pressure and PSP = peak systolic pressure; calculating volume at point ESP by integrating said flow curve throughout the ejection phase of the patient's heart, and viewing said PVL on a monitor screen.

The invention further provides a system for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, comprising electrocardiograph means having electrodes attachable to selected points on the body of said patient; a pressurizable cuff mountable on an arm of said patient; computer means provided with display means connectable to said electrocardiograph means and to said pressurizable cuff via a pressure card, and monitoring means

locatable externally of said patient in such a position as to be capable of monitoring the aortic root of said patient's heart, the output of said means leading at least indirectly to said computer means.

The invention will now be described in connection with certain preferred embodiments with reference to the following illustrative figures so that it may be more fully understood.

With specific reference now to the figures in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

- Fig. 1 represents a PVL, including the diastolic point (DP), the peak systolic point (PSP) and the end systolic point (ESP);
- Fig. 2 shows the flow curve F (flow) vs. T (time);
- Fig. 3 is the pressure curve P (pressure) vs. T (time), including DP and PSP, and
- Fig. 4 is a block diagram of the system according to the invention.

The method according to the invention requires, in principle, the taking of two measurements, neither of them invasive: (1) measurement of instantaneous flow in the aortic root (Fig. 2) by means of a commercially available echo-Doppler device; and (2) measurement of instantaneous pressure in the aortic root (Fig. 3) by means of a pressure cuff, in combination with an ECG monitor of the well-known type, and the plotting of flow and pressure curves yielded by these measurements.

The invention resides in the way data from these two measurements are combined to yield the PVL, the curve representing pressure vs. volume, as well as in the derivation of cardiac power and contractile reserve from these non-invasive measurements.

Referring now to the drawings, there is shown in Fig. 1 a complete PVL, seen to consist of five segments a, b, c, d and e.

Segment a, representing the filling of the heart with blood, is approximated by a linear curve with a predetermined empirical slope which is easily found in the literature.

Segment b, representing the phase in which the heart contracts, pressure rises and the aortic valve opens (at point 1) when diastolic pressure has been reached, is a straight, vertical line leading from segment a to the diastolic point DP (point 1), at an abscissa of EDV (end diastolic volume).

Segment c, representing that phase of the cardiac cycle in which blood is ejected into the arteries, with pressure starting from DP and reaching its peak at point 2 (peak

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systolic point - PSP), also represented in the P vs T curve of Fig. 3, is the clinically most important section of the PVL.

Segment d represents that part of the cycle in which pressure drops from PSP to EPS (end systolic point), i.e., from point 2 to point 3. It is approximated by a straight line.

Segment e, a vertical line starting at ESP (point 3), represents that part of the cycle in which the heart muscle fully relaxes, resulting in an immediate pressure relief. Segment e joins segment a above point ESV (end systolic volume) on the abscissa.

While segments b, d and e are easily constructed, being straight lines, and segment a can be found in the literature, segment c is a function of several parameters, the determination of which is described further below.

Cardiac power represents the product of cardiac systolic flow and cardiac systolic pressure, as shown in the following equation:

$$\text{Cardiac power} = \text{flow}_{\text{sy}} \times \text{pressure}_{\text{sy}} \quad (1)$$

where:

flow_{sy} is aortic flow, computed from the velocity/time integral x aortic valve area measured in the apical four-chamber view by echo-Doppler, and
 $\text{pressure}_{\text{sy}}$ is central aortic pressure measured by the invention, as described above and below.

Cardiac peak power represents the maximal product of the above equation:

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$$\text{Peak power} = \max(\text{flow}_{\text{sys}} \times \text{pressure}_{\text{sys}}) \quad (2).$$

As stated above, recent experimental data indicate that peak power is an index of contractility. Contractile reserve can thus be calculated by measuring cardiac power at rest and under maximal stress, and calculating the difference:

$$\text{Contractile reserve} = \text{peak power}_{\text{max}} - \text{peak power}_{\text{rest}} \quad (3).$$

As mentioned above, calculation of the PVL, cardiac power and contractile reserve, is made possible by two non-invasive measurements: the measurement of instantaneous flow at the aortic root, and the measurement of instantaneous pressure at the aortic root.

These measurements are described below in conjunction with Fig. 4.

In the block diagram of Fig. 4, the patient is connected to a standard electrocardiograph (ECG) 2 and wears a slightly modified pressure cuff 4 of the type used in blood-pressure measurements.

To establish the flow curve (Fig. 2), probe 6 of a per se known echo-Doppler device (EDD) 8 is placed in an apical four-chamber position so that it can "view" the aortic root. Velocity waves emerging from the aortic root are imaged on display screen 10 when the EDD is in the Doppler mode. Flow can then be calculated from the expression:

$$\text{Flow} = \text{velocity} \times \text{valve area}.$$

Simultaneously with the display of the flow waves, the technician runs a commercially available video image

grabbing program (VIG), installed together with the appropriate video card 12.

Using the VIG program with the EDD, the technician selects a frame that displays the velocity wave to best advantage. This frame is then recorded by VCR 14 and stored in the memory of computer 16 or other electronic means, for subsequent processing.

While in the preferred embodiment of the invention an echo-Doppler device is used to record blood flow velocity at the aortic root, the same purpose can be achieved by using a per se known gamma-camera, or any equivalent equipment which replaces the EDD 8, the VCR 14 and the video card 12.

For processing, the technician runs a flow-analysis program (FA) that guides him through the following steps:

1. The selected flow image is displayed on the screen of PC monitor 18.
2. The technician marks the region of interest within the displayed flow wave.
3. The FA program automatically detects the flow wave contour and stores it as a series of data points, consisting of pairs of flow and time.
4. The time is estimated by the FA program by detecting the QRS complex of the ECG pattern displayed as a standard feature on the EDD flow image. The time of each data point is estimated relative to the QRS complex, in milliseconds.

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5. The FA program then loads the stored data points, and, using a polynomial 4th degree fit, generates a flow curve accurately resembling the original flow wave.
6. The flow curve is stored on the computer disk for further processing.

To establish the pressure curve, a device is used to non-invasively measure the pressure at the aortic root which, in the form of pressure card 20, simultaneously receives input from ECG monitor 2 and pressure cuff 4.

The procedure is as follows:

1. Cuff 4 is placed on the patient's arm above the brachial artery and inflated to a pressure exceeding the peak systolic pressure of the patient. At that pressure, flow in the brachial artery completely stops.
2. Cuff 4 is allowed to deflate at a controlled rate, with pressure inside cuff 4 being measured on-line throughout deflation.
3. Card 20 is connected to the sync output of monitor 2, and recordings are made of the internal clock time of computer 16, as well as of the QRS complexes detected by monitor 2.
4. A sensor (possibly based on sound, flow, pressure, magnetic detection, etc.), placed inside, proximal or distal to cuff 4, is used to detect, during deflation, blood flow penetrating the barrier constituted by the pressure cuff. Such penetration occurs the moment brachial pressure equals or slightly

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exceeds cuff pressure. It is a proven scientific fact that, at this point, pressure in the brachial artery equals the pressure in the aortic root, hence it equals the pressure in cuff 4.

5. As the QRS complex, cuff penetration point and internal clock time are sampled simultaneously and on-line, time between the QRS complex and cuff penetration can be measured and stored.
6. As the pressure in cuff 4 decreases, the time to cuff penetration decreases until the patient's diastolic pressure is reached, where the time becomes constant. A series of data points is generated from peak systolic to diastolic pressure, each consisting of cuff pressure at penetration coupled with the time of their occurrence after the corresponding QRS complex. The data points are stored for further processing.
7. For processing the recorded data, a pressure analysis program (PA) is run, which loads the stored data points and, using a polynomial 4th degree fit, generates a pressure curve accurately resembling the ascending limb of the aortic pressure wave.
8. The pressure curve (Fig. 3) and the flow curve (Fig. 2) are analyzed at the corresponding instantaneous time point.
9. The pressure value (P) is taken from the pressure curve.
10. The volume value (V) is calculated by integrating instantaneous flow up to that time point.

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11. Points P and V are presented in the diagram in order to draw segment c up to PSP (point 2, Fig. 1).
12. The curve between PSP and ESP (point 3, Fig. 1) is approximated by a straight line.
13. Pressure at point ESP is calculated, using the expression:
$$ESP = DP + 2/3 (PSP - DP).$$
14. Volume at point ESP is calculated by integrating the flow curve throughout the ejection phase.
15. Finally, pressure and flow curves are aligned by synchronization to ECG signals, thus allowing calculation of instantaneous cardiac power. From the power curves, peak power and contractile reserve are obtained.

Also provided are such further peripherals as a data base 22 and a printer 24.

While according to Fig. 4 the image produced by the echo-Doppler device 8 is transferred to computer 16 via VCR 14 and video card 12, an embodiment is envisaged in which the EDD signals producing this image will be directly transferred to computer 16, obviating the need for VCR 14 and video card 12.

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrated embodiments and that the present invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof. The present embodiments are therefore to be considered in all respects

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as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A method for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, comprising the steps of:

connecting said patient to an electrocardiograph;

mounting the probe of an echo-Doppler device on the patient in a position enabling it to sense the aortic root and to produce signals representative of the flow waves issuing from said aortic root;

analyzing said signals and obtaining a series of data points as pairs of flow and time, using the QRS complex of the electrocardiogram pattern as a time reference point;

applying a curve-fitting procedure to turn said data points into a flow curve resembling the flow wave issuing from said aortic root;

placing a pressure cuff on the patient's arm and inflating it to a point where all flow in the patient's brachial artery stops;

deflating said cuff at a controlled rate while measuring pressure inside said cuff throughout deflation;

during deflation, sensing blood flow penetrating the barrier constituted by said pressurized cuff, with instantaneous pressure at the aortic root being equal to instantaneous pressure inside said cuff;

obtaining a series of data points from peak systolic to diastolic pressure, each point consisting of cuff pressure at penetration coupled with the time of its occurrence after the corresponding QRS complex;

applying a curve-fitting procedure to turn said data points into a pressure curve resembling the ascending limb of the aortic pressure wave;

calculating the end systolic pressure (ESP) using the expression

$$ESP = DP + 2/3 (PSP - DP)$$

where:

DP = diastolic pressure, and

PSP = peak systolic pressure;

calculating volume at point ESP by integrating said flow curve throughout the ejection phase of the patient's heart, and

viewing said PVL on a monitor screen.

2. The method as claimed in claim 1, comprising the further step of calculating at least one of the parameters cardiac power, cardiac peak power and contractile reserve, using the expressions:

$$\text{Cardiac power} = \text{flow}_{\text{ay}} \times \text{pressure}_{\text{ay}}$$

where:

flow_{ay} = aortic flow computed from the velocity/time integral x aortic valve area measured in the apical four-chamber view by echo-Doppler, and

$\text{pressure}_{\text{ay}}$ = the central aortic pressure;

$$\text{Cardiac peak power} = \max(\text{flow}_{\text{ay}} \times \text{pressure}_{\text{ay}})$$

i.e., the maximum product of flow_{ay} and $\text{pressure}_{\text{ay}}$, and

$$\text{Contractile reserve} = \text{peak power}_{\text{max}} - \text{peak power}_{\text{rest}}$$

i.e., the difference between peak power under maximal stress and peak power at rest.

3. The method as claimed in claims 1 and 2, comprising the further step of storing all data yielded by said method in a data bank.

4. The method as claimed in claim 1, comprising the further step of producing a print-out of said PVL as calculated and as imaged on said display means.

5. The method as claimed in claim 1, wherein said signals are produced by an echo-Doppler device and are utilized to generate an image on a CRT screen.

6. The method as claimed in claim 5, comprising the further step of using a VCR to record the image produced by said echo-Doppler device and to transfer said image via a video card to said computer means.

7. A system for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, comprising:
 electrocardiograph means having electrodes attachable to selected points on the body of said patient;

 a pressurizable cuff mountable on an arm of said patient;

 computer means provided with display means, connectable to said electrocardiograph means and to said pressurizable cuff via a pressure card, and

 monitoring means locatable externally of said patient in such a position as to be capable of monitoring the aortic root of said patient's heart, the output of said means leading, at least indirectly, to said computer means.

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8. The system as claimed in claim 7, wherein said monitoring means is an echo-Doppler device having a probe mountable on selected points on the body of said patient and leading, at least indirectly, to said computer means.

9. The system as claimed in claim 7, wherein said monitoring means is a gamma-camera, the output of which leads, at least indirectly, to said computer means.

10. The system as claimed in claim 7, wherein said pressurizable cuff is provided with at least one sensor responsive to blood flow in the patient's brachial artery penetrating the barrier constituted by said cuff.

11. The system as claimed in claim 8, wherein said echo-Doppler device comprises a display screen.

12. The system as claimed in claim 11, further comprising a VCR adapted to record the image on said display screen and to transfer image signals via a video card to said computer means.

13. The system as claimed in claim 7, further comprising a data base communicating with said computer means.

14. The system as claimed in claim 7, further comprising a printer addressable by said computer means.

15. A method for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, substantially as hereinbefore described and with reference to the accompanying drawings.

16. A system for the non-invasive determination of the pressure-volume loop (PVL) of a patient's heart, substantially as hereinbefore described and with reference to the accompanying drawings.

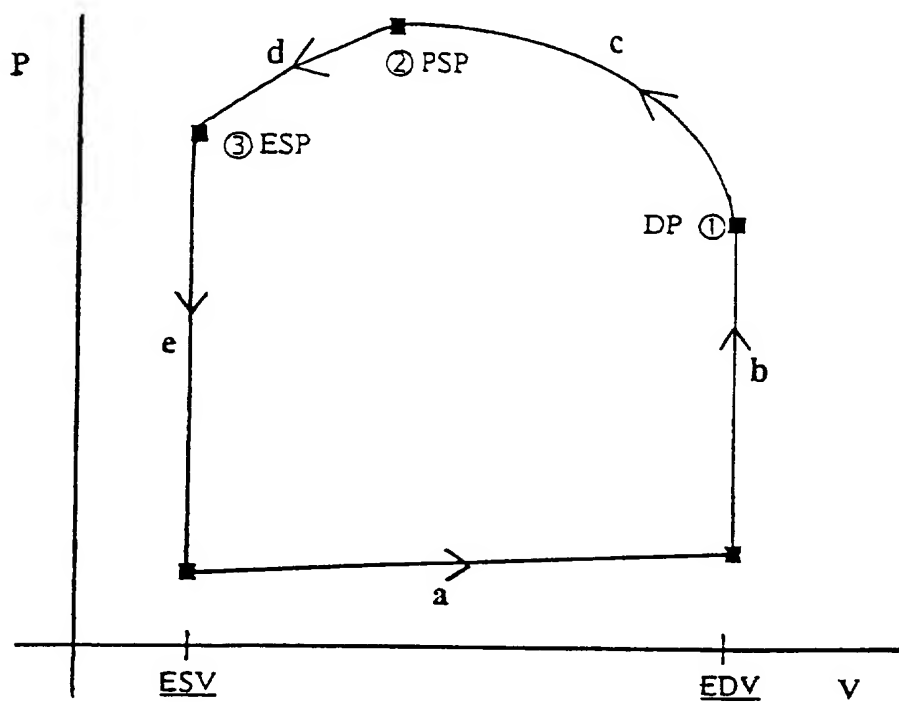


Fig. 1

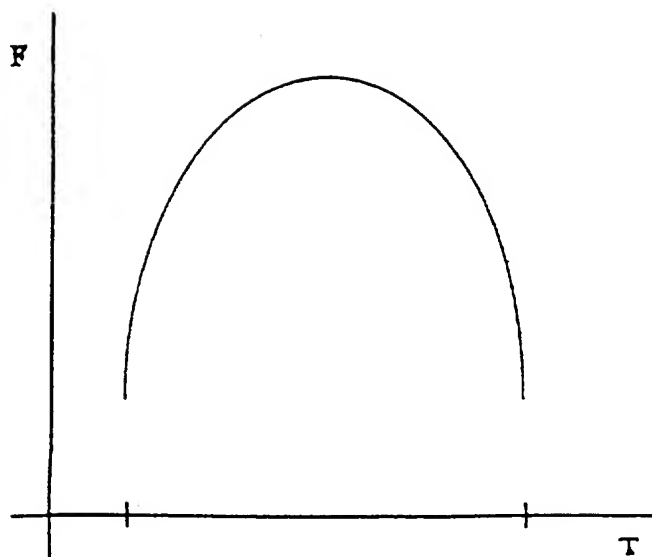


Fig. 2

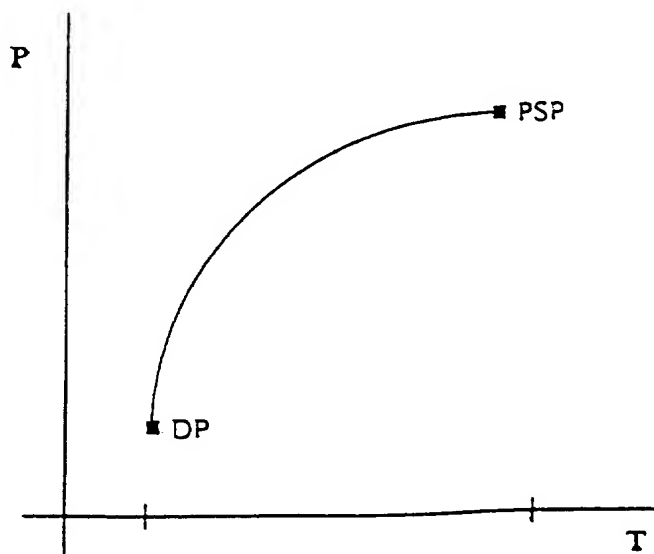


Fig. 3

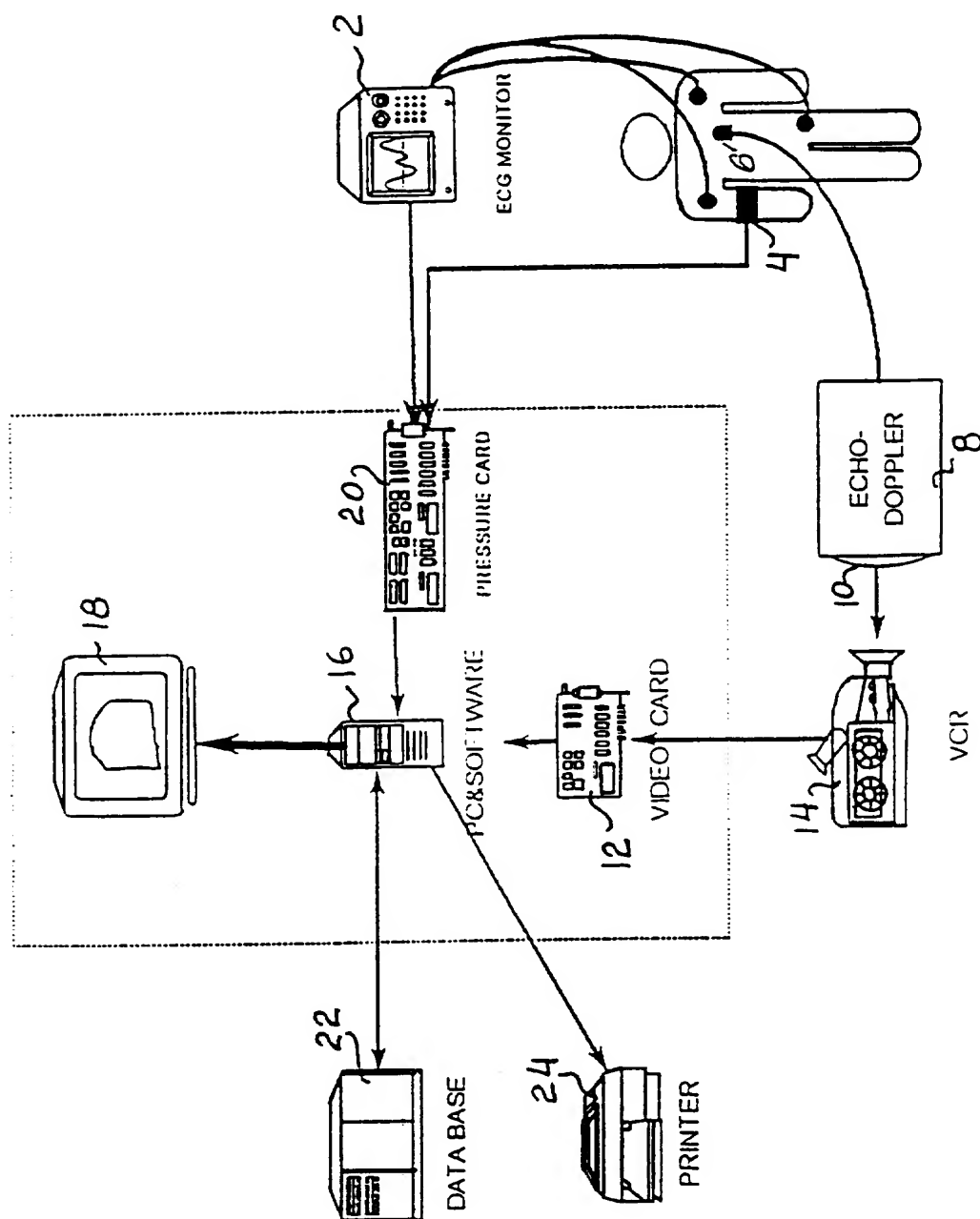


Fig. 4

INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/IB 96/01052

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61B5/029 A61B5/0205 A61B8/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	EP,A,0 651 970 (ROBIN MEDICAL TECHNOLOGIES) 10 May 1995 see column 2, line 35 - column 8, line 14; tables 1-7	1,3,5, 15,16 2,7-10, 13
A	--- WO,A,91 13589 (PRECISION DIAGNOSTICS, INC.) 19 September 1991 see page 13, line 5 - page 25, line 13; tables 1-12	1-3,5,7, 8,10, 13-16
A	--- WO,A,94 10903 (H.KUNIG ET AL) 26 May 1994 see page 8, line 21 - page 10, line 10; tables 1-3 -----	1,2,4,14



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Patent family members are listed in annex.

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Date of the actual completion of the international search

9 January 1997

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-651970	10-05-95	JP-A- 7184868	25-07-95
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WO-A-9410903	26-05-94	US-A- 5370122	06-12-94
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